ISIS-4682 70 **PATENT**

ABSTRACT OF THE DISCLOSURE

The present invention is directed to improved methods and compositions for synthesis of oligonucleotides and other phosphorus-linked oligomers, without the need for phosphoryl protecting groups. The methods involve the reaction of nucleoside phosphoramidites with a support-bound oligomer having one or more unprotected phosphorus-containing internucleoside linkages in the presence of a neutralizing agent.